

DOCKET NO. 9491-058-27

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

IN RE APPLICATION OF: THOMAS R. GADEK, ET AL.

SERIAL NO.: NEW APPLICATION

FILING DATE: HERewith

FOR: IDENTIFICATION OF NON-COVALENT COMPLEXES BY MASS  
SPECTROMETRY

**PRELIMINARY AMENDMENT**

ASSISTANT COMMISSIONER FOR PATENTS  
WASHINGTON, D.C. 20231

SIR:

Prior to examination of the above-identified application, and to advance the prosecution thereof, please amend the above-referenced application in the following manner.

**IN THE CLAIMS**

Please amend the claims as follows:

4. (Amended) The method of claim 2, wherein the identified linked ligands have a disassociation constant,  $K_d$ , equal to 500 mM or less.
5. (Amended) The method of claim 1, wherein the first binding site is the same as the second binding site.
6. (Amended) The method of claim 1, wherein the first binding site is not the same as the second binding site.

107307-021202

7. (Amended) The method of claim 1, wherein assembling step (b) comprises determining binding of target binding ligands to the target having at least one member of the first set of target binding ligands bound thereto.

8. (Amended) The method of claim 1, wherein the target is a target biomolecule.

10. (Amended) The method of claim 1, wherein step (c) comprises forming a covalent bond linking the member of the first set and the member of the second set.

11. (Amended) The method of claim 1, wherein screening step (d) comprises a biological measurement.

12. (Amended) The method of claim 1, wherein a member of the first set and a member of the second set bind to the target in a 1:1 ratio.

13. (Amended) The method of claim 1, further comprising assembling a third set of target binding ligands that compete for binding to the first binding site on the target and a fourth set of target binding ligands that compete for binding to the first binding site on the target, where members of each of the third set and the fourth set compete with members of the first set for binding to the first binding site, but members of the third set do not compete with members of the fourth set for binding to the target.

14. (Amended) The method of claim 13, further comprising covalently linking at least one member of the third set or the fourth set and at least one member of the second set to provide a second set of linked ligands; and screening the second set of linked ligands to identify members thereof that bind to the target.

17. (Amended) The method of claim 15, wherein the first binding site is not the same as the second binding site.

18. (Amended) The method of claim 15, further comprising screening the set of linked ligands to identify members thereof that bind to the target.

19. (Amended) The method of claim 15, further comprising covalently linking at least one member of a third set of target binding ligands that compete for binding to the first binding site on the target or at least one member of a fourth set of target binding ligands that compete for binding to the first binding site on the target to form a second set of linked ligands, where members of each of the third set and the fourth set compete with members of the first set for binding to the first binding site, but members of the third set do not compete with members of the fourth set for binding to the target.

20. (Amended) A method for inhibiting the binding of a second biomolecule to a first biomolecule, comprising:

contacting the first and second biomolecules with a binding inhibitory amount of a compound identified according to claim 1, where the compound binds to the first biomolecule and inhibits the binding of the second biomolecule.

#### REMARKS

The claims have been amended to correct the improper multiple dependencies. Accordingly, no new matter has been added and entry of the amendments is respectfully requested.

Applicants respectfully submit that this application is in condition for allowance and request favorable consideration.

If any points remain at issue which can best be resolved by way of a telephonic or

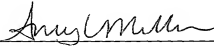
personal interview, the Examiner is kindly requested to contact the undersigned attorney at the local telephone number listed below.

Respectfully submitted,

PIPER MARBURY RUDNICK & WOLFE

2/12/02

Date



Steven B. Kelber  
Registration No: 30,073  
Attorney of Record

Amy L. Miller  
Registration No: 43,804

1200 Nineteenth Street, N.W.  
Washington, D.C. 20036-2412  
Telephone: (202) 861-3900  
Facsimile : (202) 223-2085

10073077-021202

**MARKED-UP COPY OF AMENDED CLAIMS**

4. (Amended) The method of claim 2 [or 3], wherein the identified linked ligands have a disassociation constant,  $K_d$ , equal to 500 mM or less.

5. (Amended) The method of [any of the previous claims] claim 1, wherein the first binding site is the same as the second binding site.

6. (Amended) The method of [any of the previous claims] claim 1, wherein the first binding site is not the same as the second binding site.

7. (Amended) The method of [any of the previous claims] claim 1, wherein assembling step (b) comprises determining binding of target binding ligands to the target having at least one member of the first set of target binding ligands bound thereto.

8. (Amended) The method of [any of the previous claims] claim 1, wherein the target is a target biomolecule.

10. (Amended) The method of [any of the previous claims] claim 1, wherein step (c) comprises forming a covalent bond linking the member of the first set and the member of the second set.

11. (Amended) The method of [any of the previous claims] claim 1, wherein screening step (d) comprises a biological measurement.

12. (Amended) The method of [any of the previous claims] claim 1, wherein a member of the first set and a member of the second set bind to the target in a 1:1 ratio.

13. (Amended) The method of [any of the previous claims, wherein] claim 1, further [comprises] comprising assembling a third set of target binding ligands that compete for binding to the first binding site on the target and a fourth set of target binding ligands that compete for binding to the first binding site on the target, where members of each of the third set and the fourth set compete with members of the first set for binding to the first binding site, but members of the third set do not compete with members of the fourth set for binding to the target.

14. (Amended) The method of claim 13, further [comprises] comprising covalently linking at least one member of the third set or the fourth set and at least one member of the second set to provide a second set of linked ligands; and screening the second set of linked ligands to identify members thereof that bind to the target.

17. (Amended) The method of claim 15 [or 16], wherein the first binding site is not the same as the second binding site.

18. (Amended) The method of [any of claims 15-17] claim 15, further [comprises] comprising screening the set of linked ligands to identify members thereof that bind to the target.

19. (Amended) The method of [any of claims 15-18] claim 15, further [comprises] comprising covalently linking at least one member of a third set of target binding ligands that compete for binding to the first binding site on the target or at least one member of a fourth set of target binding ligands that compete for binding to the first binding site on the target to form a second set of linked ligands, where members of each of the third set and the fourth set compete with members of the first set for binding to the first binding site, but members of the third set do not compete with members of the fourth set for binding to the target.

20. (Amended) A method for inhibiting the binding of a second biomolecule to a first biomolecule, comprising:

contacting the first and second biomolecules with a binding inhibitory amount of a compound identified according to [any of claims 1-19] claim 1, where the compound binds to the first biomolecule and inhibits the binding of the second biomolecule.

10073077.021202